UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,406	06/24/2003	Pier Andrea Borea	PAT-0040-US-NP2	4184

57999 7590 11/29/2007

KING PHARMACEUTICALS, INC.
400 CROSSING BOULEVARD
BRIDGEWATER, NJ 08807

EXAMINER
GEMBEH, SHIRLEY V

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/603,406	BOREA ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,8,11-16,19 and 28-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,11-16,19 and 28-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The finality of the action dated 8/24/07 have been withdrawn.

The response filed **11/15/07** presents remarks and arguments to the office action mailed **8/24/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 11/15/07 is acknowledged and has been reviewed.

Status of Action

Claims 7-8, 11-16, 19 and 28-42 are examined. Claims 1-6, 18 and 20-27 are cancelled and claims 33-42 are newly added. Claims 7 -8, 12, 19 and 28-32 are currently amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8, 11-16, 19 and 28-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 7, recites the term "suppressing" MDR. Nowhere in the specification is there a mention of "suppressing".

Maintained Claim Rejections - 35 USC § 103 revised with new claims

Applicant submits in reference to a communication submitted 10/3/06 , relying on the unexpected result of the enhancement illustrated in the Tables 4-8.

In response, the data set forth is not convincing, if one looks at the data keenly, the concentration of paclitaxel is from 0.002-0.1 µg/ml and the concentration of the A3 antagonist is either 10 µg/ml almost a 100 fold increase as shown in Table 4 for example . Giving that both A3 antagonist and antineoplastic inhibits cancer, (known to one of ordinary skill in the art). See enclosed reference as cited to show that A3 inhibits cancer

(Fishman et al. European J. Cancer 36(2000) 1452-1458) See Abstract. Fisherman et al. teaches low dose of adenosine and other small molecules. It appears in the instant application that the concentration of the antagonist has replaced the amount of the other drugs such as paclitaxel. In order for synergism to be effective, one of ordinary skill in the art would like to know how each of the drugs individually affect the cancer, especially when it has been shown in the art that both are used for cancer treatment.

Based on the reasons given above, the rejection is maintained and repeated below inclusive of the newly added claims.

Claims 7-8, 11-16, 19 and 28-42 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,210,917 to Carson et al. in view of Jacobson et al. US Patent No. 6,066,642 and further in view of Baraldi et al., Journal of Medicinal Chemistry. Vol. 42 (1999) 4473-4478 (all of record) and Goodman and Gilman, The pharmacological Basis of Therapeutics.

Carson et al. teach an adenosine-5'- triphosphate depleting agent to treat cancers such as breast and colon cancer (see col.12 lines 53-55) that are multidrug resistant, MDR, (see Abstract) in combination with chemotherapeutic agents. See col. 2, lines 37-40 and with respect to vinca alkaloids, taxanes and antibiotics, see col. 1 lines 46-51. Carson et al. additionally explain that the depletion of AMP and ATP negatively affects P-glycoprotein activity, which is linked to MDR as required by instant

claims 7-8 and 12. The generality of claims 13-16, 28-31 and 34-33 and 39-42 is taught. One of ordinary skill in the art would use the different types of chemotherapeutic agents etc., based on the type of cancer. Theses are antineoplastic agents well known in the art and has been used with different drug combination to treat cancer.

Jacobson et al. teach the use of adenosine A3 receptor antagonists in the killing of cancer cells (in current claim 7; see col. 63 Example 31) wherein the A3 receptor antagonists are used alone or in combination with other active agents (see col. 16 lines 11-18).

Jacobson et al. do not specifically teach the use of a compound MRE3008F20 of the instant claims, for example.

Baraldi et al. teach MRE3008F20 is an adenosine A3 receptor antagonists (in current claims 7-8, 33 and 38; see page 4476 compound #7).

Although, the use of the term synergism is not explicitly used, Goodman and Gilman teach the combination therapy, using a drug with known other anticancer agents. See pages 1225 and 1230 with asterisks.

The motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07

Applicant argues that the claimed invention was not obvious individually analyzing the references and that the Examiner's opinion that reduction in adenosine levels would be efficacious in the treatment of cancer is nowhere reported.

This is found nonpersuasive. Even, though Carson et al. do not teach synergism explicitly, combination therapy comprising an adenosine-5'-triphosphate- depleting agent to treat cancers that are multidrug resistance is taught. See col. 2, lines 37-40. Jacobson et al. teach adenosine A3 receptor antagonists are used in combination with other active agents, motivating one of ordinary skill in the art to use other known chemotherapeutic agents for the purpose of treating cancer. Combination therapy with new drugs and existing drugs is well known in the art as taught by Goodman and Gilman (see enclosed document especially pages1225 and 1230 with astericks).

Further, to remedy the deficit drawn to the specific compound, Baraldi teaches MRE3008F20 is an adenosine A3 receptor antagonist, the specific A3 receptor antagonist claimed thus providing one of ordinary skill in the art motivation to combine the teachings of Jacobson. Applicants argue there is no suggestion to combine the references. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Applicant's arguments have been fully considered but they are not persuasive. The rejection is maintained as in the last office action of record. However, The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve

their expected results when combined for their common known purpose. Section MPEP 2144.07

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SVG
11/20/07

Ardin H. Marschel 11/26/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER